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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,894	12/15/1999	MARC PIECHACZYK	19141-007	5731

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,894	PIECHACZYK ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44,45,47,49-53,55 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44, 45, 47, 49-53, 55, 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 13, 2004 has been entered.

DETAILED ACTION

This application is a 371 national stage filing of PCT/FR98/00081, filed January 16, 1998 which claims benefit to foreign application FR 97/00540, filed January 20, 1997 in France.

Applicants' amendment filed January 25, 2005 has been received and entered. Claims 1-43, 46, 48, 54, 56 have been canceled. Claims 44, 47, 51, 52, 55, 57 and 59 have been amended. Claims 44, 45, 47, 49-53, 55, 57-59 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44, 45, 47, 49-53, 55, 57-59 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The amendment to the claims to delete "the genetically modified cell does not cause disease in the subject following transplantation" considered new matter, has addressed the basis of the rejection.

Claims 44, 51, 52 and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the embodiment wherein the cell produces "a concentration exceeding 100ng/ml of serum" is considered new matter. In review of the specification for support for the claim, it is noted that there is no literal support for claim set forth as a general inventive concept of the invention. One specific example, page 15, section IV-In vivo experiment, provides evidence that one specific cell type, with a specific construct, delivered in a particular model system provided elevated levels of "approximately 100ng/ml serum in 3 of 4 mice tested" (emphasis added). However, another table (Table 2) of other cell lines used/made provide only *in vitro* data where the amounts made appear to be much less than required by the instant claims.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 44, 51, 52 and 59 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As discussed above, the specification fails to provide the necessary and specific guidance that would provide the limitation of 100ng/ml serum for the breadth of any cell in any intended circumstance. It is noted that the product claim is directed to a genetically modified cell, and while it would be interpreted to encompass multiple cells, the specification fails to provide any guidance to what number of cells would provide the specifically claimed concentration, or even by what parameters it would be tested (i.e. time after implant measured).

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44, 45, 47, 49-53, 55, 57-59 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claims 44 and 52 have been amended to delete the embodiment of "suitable for the introduction into a subject". It is noted that the claims are still dependent to some extent on the specific intended use, in particular for the ability of a cell to secrete an antibody once transplanted. For example, in the case of xeno-transplantation where a transplanted cell is quickly rejected by the host it is unclear if the cell will be capable of secreting an expressed antibody into the blood circulation. However, since only a cell is claimed, the intended use will be assessed broadly to the extent that the cell would be able to secrete an expressed antibody from the cell itself.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44, 45, 47, 49-53, 55, 57-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright *et al.* (1992)

Wright *et al.* disclose non-lymphoid cells which contain heterologous polynucleotide sequences which express and secrete an antibody (summarized in abstract and page 130-section 6). Wright *et al.* discuss the use of the antibodies for therapeutic purposes clearly indicating that the antibody can be therapeutic (page 125). Further, Wright *et al.* give guidance and provide specific methods for the use of a variety of vectors and expression systems for expressing antibodies in cells which react to both viral and cancer antigens. In the instant case, any cell depending on its use or means of delivery would meet the limitation of intended use of this embodiment because the appropriate conditions would be found to maintain the cells. Furthermore, transformed cells are capable of proliferating in the form of a tumor in animal models, thus the cells of Wright *et al.* would be maintained in mammal. It is noted that the transformed cell lines taught by Wright *et al.* are similar to those disclosed in the working examples in the instant specification.

Therefore, Wright *et al.* anticipates the claims.

Claims 44, 45, 47, 49-53, 55, 57-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevenson *et al.*

Stevenson *et al.* teach mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from the cells (see for example figure 1). Specific ScFv fragments are taught that encode portions of the antibody providing the native V_H and V_L regions unmodified. The antibody produced by Stevenson *et al.* therefore represents a native unmodified antibody molecule. The antigen to which the antibody reacts is directed to a tumor related epitopes (page 213). Further, the V_H1 portion of the sequence contains the leader

sequence allowing for the exit of the protein from the cell (see figure 2 and legend). Finally, Stevenson *et al.* teach that the vectors can be used in to express the antibody in a variety of cells, including for example muscle cells (page 216).

The vectors and cells transduced with said vectors which express an antibody as taught by Stevenson *et al.* anticipates the claims.

Claims 44, 45, 47, 49-53, 55, 57-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen *et al.* (1994) or Chen *et al.* (1996).

. Chen *et al.* teach mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from the cells (page 5932, figure 1). Chen *et al.* teaches Fab fragments does not alter the sequences that encode portions of the antibody, leaving the native V_H, C_H, C_K and V_K regions unmodified. The antibody produced by Chen *et al.* therefore represents a native unmodified antibody molecule. The antigen to which the antibody reacts is directed to a the gp120 molecule of HIV (abstract, page 5932). Further, Chen et al. teach signal leader sequences allowing for the exit of the protein from the cell (see figure 1). Further, Chen *et al.* teach signal leader sequences allowing for the exit of the protein from the cell (see figure 1). Finally, Chen *et al.* use the non-plasmacyte COS cell to demonstrate the expression of the Fab105.

Therefore, the vectors and cells transduced with said vectors which express an antibody as taught by Chen *et al.* anticipates the claims.

Conclusion

No claim is allowed.

Newly added claims are free of the art of record because while the art of record teaches cells and methods of making non-plasmocyte cells that produce antibodies and/or antibody fragments, each of the specific cells taught would most likely form a tumor when transplanted into any subject.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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